

SCALING-UP OF ALIVIBRIO FISCHERI RECOMBINANT L-ASPARAGINASE PRODUCTION: DEVELOPING A BIOPHARMACEUTICAL INDUSTRIAL PROCESS

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Body

Among the several important steps in establishing a bioprocess, the definition of scaling-up parameters is one of the most important. The aim of this study was to evaluate the scaling up process of recombinant L-asparaginase production from orbital shaker to bioreactor, namely Stirred tank bioreactor (STR). *Alivibrio fischeri* L-Asparaginase, expressed in *Bacillus subtilis*, was produced using Luria-Bertani (LB) culture medium and xylose as inductor. Firstly, cultivations were carried out in orbital shaker using 250 mL Erlenmeyer flasks containing 50 mL of LB medium at 30 °C, 200 rpm, and following using a 6 L STR with 4 L of LB medium. Bioreactor assays were submitted to aeration of 1.5 L min⁻¹ (30% O₂). Induction time was defined considering the exponential growth phase and optimized in orbital shaker and bioreactor. After the bioprocess, cells were recuperated by centrifugation and submitted to ultrasound sonication for cell lysis. The enzymatic extract was evaluated regarding L-Asparaginase activity in the L-Asparagine hydrolysis and further released ammonium quantification by Nessler colorimetric method. Similar activities were obtained on both scales (1.427 and 1.539 U mL⁻¹ for orbital shaker and bioreactor, respectively). Growth curve revealed that bioreactor cultivation achieved maximum cell concentration in a shorter time, making it possible to increase productivity. The results showed that the proposed process have potential for industrial application, with increased productivity and without enzymatic activity losses. **Acknowledgements**

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Palavras-chave : Biopharmaceutical, Recombinant L-asparaginase, scale-up, Stirred tank bioreactor, Bioprocess